Figure 1

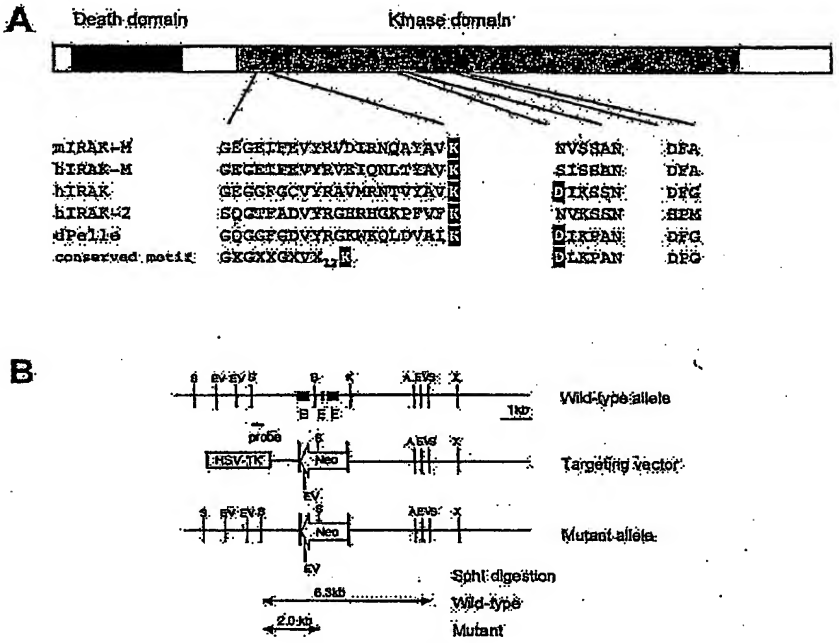

A
Death domain
Kinase domain
mIRAK-M
hIRAK-M
hIRAK
hIRAK-2
dPelle
conserved motif
B
Wild-type allele
Targeting vector
Mutant allele
probe
HSV-TK
Neo
1kb
SphI digestion
6.3kb
2.0kb
Wild-type
Mutant
C
+/+ +/- -/-
Wild-type
Mutant
D
+/+ -/-
Irak-M
HPRT

Figure 2.

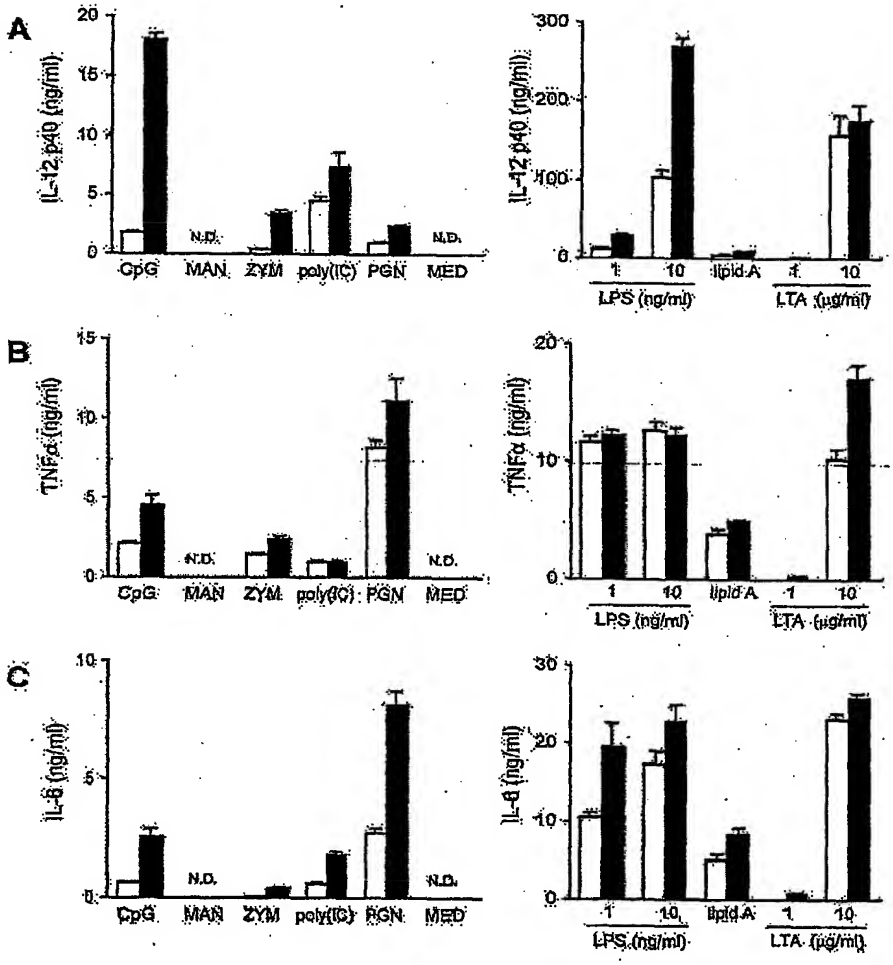
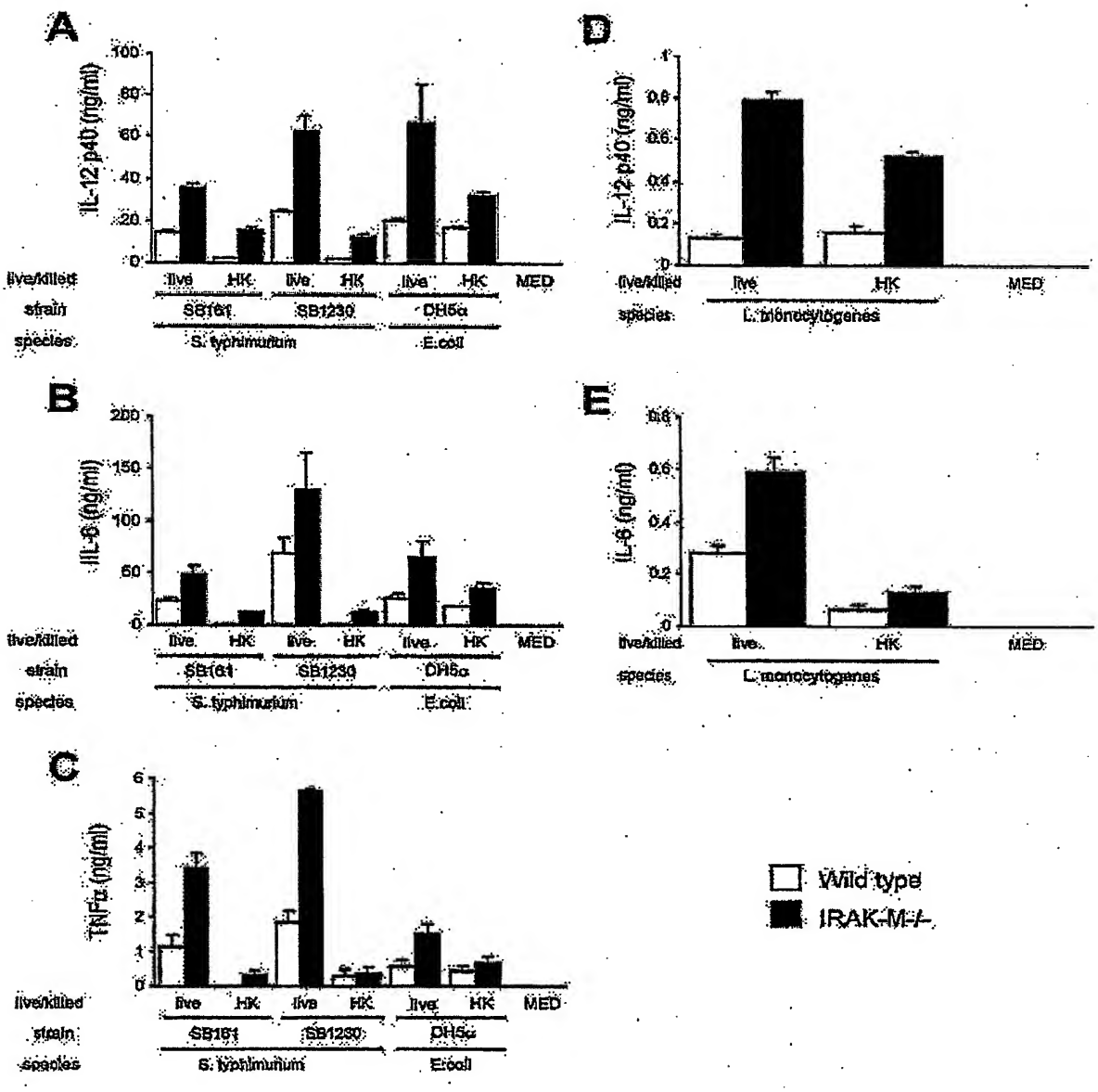

A
IL-12 p40 (ng/ml)
20
15
10
5
0
N.D.
N.D.
CpG
MAN
ZYM
poly(IC)
PGN
MED
300
200
100
0
1
10
lipid A
1
10
LPS (ng/ml)
LTA (μg/ml)
B
TNFα (ng/ml)
15
10
5
0
N.D.
N.D.
CpG
MAN
ZYM
poly(IC)
PGN
MED
20
10
0
1
10
lipid A
1
10
LPS (ng/ml)
LTA (μg/ml)
C
IL-6 (ng/ml)
10
5
0
N.D.
N.D.
CpG
MAN
ZYM
poly(IC)
PGN
MED
30
20
10
0
1
10
lipid A
1
10
LPS (ng/ml)
LTA (μg/ml)

Fig. 3


A
IL-12 p40 (ng/ml)
live/killed
strain
species
live
HK
SB161
SB1230
DH5α
S. typhimurium
E.coli
MED
B
IL-6 (ng/ml)
C
TNFα (ng/ml)
D
L. monocytogenes
E
Wild type
IRAK-M-/-

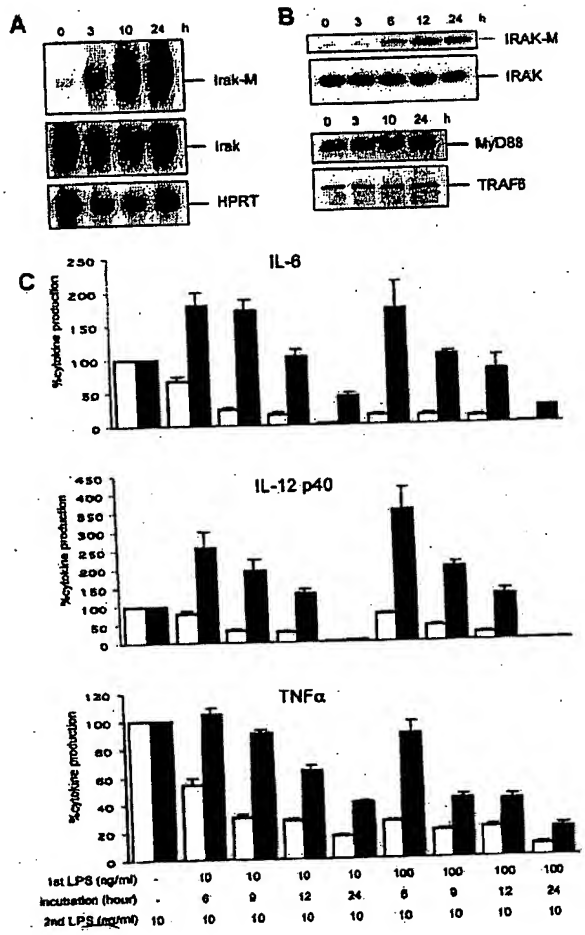

A
0 3 10 24 h
Irak-M
Irak
HPRT
B
0 3 6 12 24 h
IRAK-M
IRAK
0 3 10 24 h
MyD88
TRAF6
C
IL-6
%cytokine production
250
200
150
100
50
0
IL-12 p40
%cytokine production
450
400
350
300
250
200
150
100
50
0
TNFα
%cytokine production
120
100
80
60
40
20
0
1st LPS (ng/ml) - 10 10 10 10 100 100 100 100
Incubation (hour) - 6 9 12 24 6 9 12 24
2nd LPS (ng/ml) 10 10 10 10 10 10 10 10 10

Figure 4

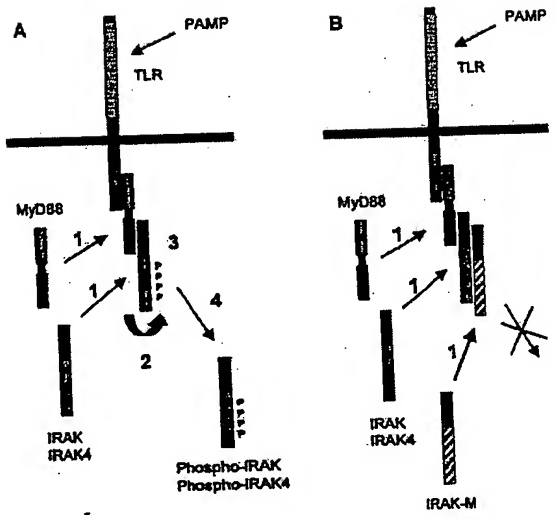

A
PAMP
TLR
MyD88
1
1
3
4
2
IRAK
IRAK4
Phospho-IRAK
Phospho-IRAK4
B
PAMP
TLR
MyD88
1
1
1
IRAK
IRAK4
IRAK-M

Figure 5